

Amendments to the Claims

Please cancel Claims 47, 49, 55 and 64-65. Please amend Claims 1, 4, 45-46, 48, 50-53, 56 and 61-63. Please add Claim 66. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

1. (currently amended): A method of stimulating bone growth in a subject at a site in a subject in need of osteoinduction bone growth and at which bone growth would not occur at said site if left untreated, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, wherein said agonist is a polypeptide of between 12 and 23 amino acids in length and is represented by the following structural formula:

Arg-Gly-Asp-Ala-R,

wherein Asp-Ala-R is a serine esterase conserved sequence.

- 2-3. (cancelled)

4. ² (currently amended): The method of Claim 1, A method of stimulating bone growth at a site in a subject in need of osteoinduction, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, comprises a peptide represented by the following structural formula:

Asp-Ala-R,

wherein R is a serine esterase conserved sequence comprising the amino acid sequence Cys-X₁-Gly-Asp-Ser-Gly-Gly-Pro-X₂-Val (SEQ ID NO: 2), of SEQ ID NO: 2 (Cys-X₁-Gly-Asp-Ser-Gly-Gly-Pro-X₂-Val, wherein X₁ is Glu or Gln and X₂ is Phe, Met, Leu, His or Val), or a C-terminal truncated fragment of SEQ ID NO: 2, said fragment having at least six amino acids.

5-44. (cancelled)

~~45.~~ ⁴ (currently amended): The method of Claim 1 ~~Claim 4~~, wherein the site is in need of a bone graft.

~~46.~~ ⁵ (currently amended): The method of Claim 1 ~~Claim 4~~, wherein the site is a segmental gap in a bone, a bone void or at a non-union fracture.

47. (cancelled)

~~48.~~ ⁶ (currently amended): The method of Claim 1 ~~Claim 47~~, wherein the peptide comprises a C-terminal amide.

49. (cancelled)

~~50.~~ ¹¹ (currently amended): The method of Claim 1 ~~Claim 49~~, wherein the peptide comprises the amino acid sequence Arg-Gly-Asp-Ala-Cys-X₁-Gly-Asp-Ser-Gly-Gly-Pro-X₂-Val (SEQ ID NO: 4), wherein X₁ is Glu or Gln and X₂ is Phe, Met, Leu, His or Val.

~~51.~~ ⁷ (currently amended): The method of Claim 48, wherein the peptide comprises the amino acid sequence ~~Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val~~ Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO: 5); ~~or an N-terminal truncated fragment thereof, provided that zero, one or two amino acids at positions 1-9 in the agonist are conservative substitutions of the amino acid at the corresponding position of SEQ ID NO: 5.~~

~~52.~~ ¹² (currently amended): The method of Claim 1 ~~Claim 47~~, wherein the C-terminus of the peptide is unsubstituted.

¹³
~~53.~~ (currently amended): A method of stimulating bone growth in a subject at a site in a subject in need of osteoinduction bone growth and at which bone growth would not occur at said site if left untreated, said method comprising the step of administering to the site a therapeutically effective amount of a peptide of between 12 and 23 amino acids in length comprising the sequence ~~Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val~~ Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO: 5), ~~or an N-terminal truncated fragment thereof.~~

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~~54.~~ (previously presented): The method of Claim ~~53~~¹³ wherein the peptide is C-terminal amidated.

55. (cancelled)

¹⁵
~~56.~~ (currently amended): The method of Claim 53, wherein the peptide is ~~Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val~~ Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO: 5).

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~~57.~~ (previously presented): The method of Claim ~~56~~⁷, wherein the agonist is administered in a pharmaceutical composition additionally comprising an implantable, biocompatible carrier.

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~~58.~~ (previously presented): The method of Claim ~~57~~⁸, wherein the implantable, biocompatible carrier is an osteoconductive matrix.

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~~59.~~ (previously presented): The method of Claim ~~58~~⁷, wherein the carrier comprises a polylactic acid/polyglycolic acid homopolymer or copolymer.

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60. (previously presented): The method of Claim ² 4, wherein the subject is a farm animal, a companion animal or a laboratory animal.

¹⁶
61. (currently amended): A method of stimulating bone growth in a subject at a site in need of a bone graft ~~in a subject~~, said method comprising the step of administering to the site a therapeutically effective amount of a C-terminal amidated peptide of 23 amino acids comprising the sequence ~~Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val~~ Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO: 6).

¹⁷
62. (currently amended): A method of stimulating bone growth in a subject at a segmental bone gap, a bone void or a non-union fracture, said method comprising the step of administering to the bone gap, bone void or nonunion fracture, a therapeutically effective amount of a C-terminal amidated peptide of 23 amino acids comprising the sequence ~~Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val~~ Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO: 6).

¹⁸
63. (currently amended): A method of stimulating bone growth in a subject at an ectopic site in need of bone growth and at which bone growth would not occur at said ectopic site if left untreated, said method comprising the step of administering to the ectopic site a therapeutically effective amount of a C-terminal amidated peptide of 23 amino acids comprising the sequence ~~Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val~~ Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO: 6).

64-65. (cancelled)

¹⁹
66. (new): A method of stimulating bone growth in a subject at a site in need of bone growth and at which bone growth would not occur at said site if left untreated, said method

comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor, wherein said agonist is a polypeptide of 23 amino acids in length and is represented by the following structural formula:

Arg-Gly-Asp-Ala-R,

wherein Asp-Ala-R is a serine esterase conserved sequence.